REMARKS

At the outset, Applicant would like to thank the Examiner for the courtesy of a telephonic interview on August 1, 2006, wherein amendments to the claims were discussed. The Examiner's suggestions and guidance are hereby gratefully acknowledged.

Claims 21, 22, 25, 26, 28, 29, 32, 33, 36, and 37 are pending. Claims 1-20, 23, 24, 27, 30, 31, 34, and 35 were previously canceled. Claims 21, 28, 36, and 37 are amended herein. Accordingly, claims 21, 28, 36, and 37, as amended, and dependent claims therefrom are presently under consideration.

Support for amendment to the claims is found throughout the specification and in the original claims. Specifically, support for amendment to claim 21 is found in previously presented claims 21 and 24 and, for example, in paragraph 20. Support for amendment to claim 28 is found in previously presented claims 28 and 31 and, for example, in paragraph 20. Support for amendment to claim 36 is found in Example 3, see in particular paragraphs 137-138. Support for amendment to claim 37 is found, for example, in paragraph 130 and Figure 1, wherein it is shown that administration of NB-DNJ to Sandhoff mice resulted in an ~21% increase in survival time as compared to that of untreated controls. Support for amendment to claims 21, 28, 36, and 37 is also found in paragraphs 69 and 70, wherein support for a suitable dose being an efficacious amount of material is found; and paragraphs 29 and 30, wherein support for glucosylceramide synthase as an example of an enzyme responsible for glucosylceramide synthesis is presented. No issue of new matter is introduced by these amendments.

Rejections under 35 USC § 112

Claims 21, 22, 28, and 29 stand rejected and newly added claims 36 and 37 are rejected under 35 USC § 112, first paragraph, for containing subject matter that was allegedly not described by the specification in a manner sufficient to convey that the inventor was in possession of the claimed invention at the time of filing. Claims 21, 28, 36, and 37 are amended herein to clarify the subject matter. In view of the amendments to the claims, this rejection, as it applied to claims 21, 22, 28, 29, 36, and 37 is hereby obviated.

The Examiner affirms that the specification provides a detailed description and reduction to practice using imino sugar compounds capable of inhibiting glucosylceramide

synthase enzyme. The claims are amended herein to recite that the inhibitor is an inhibitor of glucosylceramide synthase enzyme, wherein the inhibitor is an imino sugar. In view of the above, therefore, Applicant believes that the above rejection is obviated and respectfully requests that the rejection be withdrawn.

Claims 21, 22, 25, 26, 28, 29, 32, and 33 stand rejected and newly added claims 36 and 37 are rejected under 35 USC § 112, first paragraph, for allegedly failing to comply with the enablement requirement. The rejection appears to be based on a single explanation of what is meant by the term "treatment", which the Examiner has interpreted as excluding the usual meaning of the term treatment which typically relates to the alleviation of symptoms associated with a disorder. Applicant respectfully asserts that the passage in the specification does not explicitly exclude the usual above-stated meaning of the term "treatment". Nevertheless, although Applicant does not acquiesce to the Examiner's narrow interpretation of the term "treatment", the claims are amended to clarify that the methods are directed to providing symptomatic relief for a patient suffering from a mucopolysaccharide disease. In light of the amendments to the claims and Applicant's arguments presented herein, the rejection under 35 USC § 112, first paragraph, is obviated with respect to claims 21, 22, 25, 26, 28, 29, 32, and 33.

In keeping with the Examiner's narrow interpretation of the term "treatment", the Examiner views the claims as encompassing a method of preventing or curing a mucopolysaccharide disease in a patient. The Examiner maintains the position that the present specification allegedly does not present sufficient support to enable an ordinarily skilled practitioner to practice the invention with respect to claims directed to a method of preventing or curing a mucopolysaccharide disease in a patient. The Examiner does, however, acknowledge that the specification is enabled for a method comprising administering an imino sugar inhibitor of glucosylceramide synthase in an amount sufficient to provide symptomatic relief as recited in the instant claims. In that the instant claims are presently directed to methods comprising administering an imino sugar inhibitor of glucosylceramide synthase in an amount sufficient to provide symptomatic relief, Applicant asserts that the instant claims are enabled by the specification. More specifically, the claims remain directed to a method of reducing neuronal glycolipid storage in mucopolysaccharide disease in a patient afflicted with such a disease (claim 28), or to a method that relates to

reducing pathological features resulting from glycolipid accumulation in a patient with a mucopolysaccharide disease (claim 36); slowing mucopolysaccharide disease progression in an afflicted patient (claim 21); and to improving survival of a patient with a mucopolysaccharide disease (claim 37). Moreover, Applicant affirms that the examples presented in the specification attest to the fact that the instant claims are enabled by the specification.

As previously stated, Example 3 presents clear evidence demonstrating that the present method reduces neuronal glycolipid storage and reduces pathological features resulting from glycolipid accumulation in a patient with a mucopolysaccharide disease. See page 22, paragraphs 131 through to 138. These results are generated in a murine model system of MPS IIIA (Sanfilippo disease). As described in the specification, this murine model system exhibits the disorder's characteristic joint and skeletal storage of proteoglycan fragments, and neuronal storage of GM2 and GM3 gangliosides. Significantly, colonies of mutant mice expressing the MPS IIIA phenotype have been described in many peer reviewed references available in the literature and have been validated by a number of criteria as an authentic model of the disease. Indeed, as stated in the specification, MPS IIIA mice display clinical signs of the disease around 6 months of age with decreased activity, scruffy coat, abdominal distention, hunched posture and waddling gait. By 12 months, the mice exhibit severe ataxia, tremors and weight loss. Death results by 18 months or less.

Further proof as to the enablement of the claimed methods is found in Example 2 which presents results demonstrating that administration of NB-DNJ alone prolongs survival of treated animals in a mouse model for Sandhoff disease. These results also affirm that administration of NB-DNJ slows mucopolysaccharide disease progression in a patient afflicted with such a disease. In brief, untreated animals lived a maximum of 140 days, whereas animals treated with NB-DNJ survived a maximum of 170 days. This amounts to a 21% increase in longevity for Sandhoff mice treated with NB-DNJ. See paragraph 130. See also Figure 1, wherein the results of groups of untreated and NB-DNJ-treated Sandhoff mice are graphically depicted. Evidence is, therefore, presented that patients with an MPS disease that are treated using the method of the present invention display prolonged survival relative to untreated controls. Moreover, Applicant asserts that the reduced lifespan of Sandhoff mice is a consequence of mucopolysaccharide disease progression and, as shown in the instant

specification, administration of NB-DNJ slows disease progression as reflected in an increase in longevity.

In view of the above, the instant specification is both enabling of the claimed method and presents experimental evidence demonstrating reduction to practice of the claimed method.

In view of the above amendments to the claims and arguments presented herein, Applicant asserts that the rejection of the claims under 35 USC § 112, first paragraph, is untenable and respectfully requests that the rejection be withdrawn.

Fees

No additional fees are believed to be necessitated by this amendment. However, should this be an error, authorization is hereby given to charge Deposit Account No. 11-1153 for any underpayment or to credit any overpayment.

Conclusion

It is submitted, therefore, that the claims are in condition for allowance. No new matter has been introduced. Allowance of all claims at an early date is solicited. In the event that there are any questions concerning this amendment, or application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of this application may be expedited.

Respectfully submitted,

Sarah J. Fashena, Ph.D.
Agent for Applicant(s)
Registration No. 57,600

KLAUBER & JACKSON
411 Hackensack Avenue
Hackensack, New Jersey 07601
(201) 487-5800

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Enclosures: Request for Continued Examination